REMARKS

Status of the claims

New Claims 69-98 are pending upon entry of the amendments submitted herein, and all previously-submitted claims 1-68 are cancelled without prejudice or disclaimer. Support for the amendments presented herein can be found, *inter alia*, in the specification on page 20, last full paragraph; the second complete paragraph on page 23; page 30, paragraph 1; and in Tables 1 and 2.

Applicants acknowledge that rejection under 35 U.S.C. §112, first paragraph for new matter was withdrawn by the Examiner.

Claims rejections under 35 USC § 112, first paragraph (enablement) (maintained)

Rejection of Applicants' previously-pending claims under 35 USC § 112, first paragraph, for lacking enablement is maintained in the Action. Applicants respectfully submit that the claims submitted herewith overcome the asserted grounds of rejection because the pending claims recite peptides and polypeptides consisting of the specific amino acid sequences disclosed in Applicants' specification. Applicants respectfully submit that all other bases for these grounds of rejection have been overcome or rendered moot by the newly-added claims submitted herewith. Accordingly, Applicants respectfully request that the Examiner withdraw this ground of rejection.

Claims rejections under 35 USC § 102 (maintained)

Rejection of Applicants' previously-pending claims under 35 USC § 102(b) as being anticipated by the Masignani reference. Applicants respectfully submit that the claims submitted herewith overcome the asserted grounds of rejection because the pending claims recite peptides and polypeptides consisting of the specific amino acid sequences disclosed in Applicants' specification. Applicants respectfully submit that all other bases for these grounds of rejection have been overcome or rendered moot by the newly-added claims submitted herewith. Accordingly, Applicants respectfully request that the Examiner withdraw this ground of rejection.

However, in an effort to more fully respond to the asserted rejection, Applicants respectfully contend that their assessment of the cited reference does not support the asserted grounds of rejection. The cited reference, WO 02/077021 discloses almost 5000 *Streptococcus*

McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive
Chicago, IL 60606
Telephone: (312) 913-0001
Facsimile: (312) 913-0002

pneumoniae biosequences, from which one half (about 2500 sequences) are protein sequences. This can be found on the EPO sequence collection, EBI/EMBL at ftp://ftp.ebi.ac.uk/pub/databases/embl/patent/epo_prt.dat.gz.

The cited reference discloses bioinformatics analyses of this sequence information, including predictions and homology searches, in addition to cloning and knockout experiments for certain of the disclosed open reading frames (ORFs). Notably, and in contrast to Applicants' specification, WO 02/077021 provides no examples or other evidence for immunogenicity of the disclosed peptides and polypeptides, and no experimental data whatsoever supporting putative vaccine use for the disclosed peptides and polypeptides. This interpretation of the limited nature of the disclosure of WO 02/077021 is supported by the wording of the reference's Abstract, which states that "[t]he *invention* provides proteins and nucleic acid sequences for *Streptococcus pneumoniae* . . ." (*emphasis added*), and by both the Abstract and the disclosure being devoid of any mention of hyperimmune serum-reactive antigens being provided by the disclosure.

Applicants respectfully contend that WO 02/077021 should be considered for what it teaches, not what the skilled worker would understand from considering the reference in light of their specification. The cited reference teaches 432 "most preferred" ORF candidates (representing about one out of every 6 disclosed protein-encoding sequences); from this, the Office contends that these ORF candidates "show homology to the 'GBSnnn' antigens listed in Table IV of PCT/GB01/04789 and are thus inferred to be useful antigens for immunization and/or diagnosis." However, when the secondary reference is examined, it contains sequences not from *Streptococcus pneumoniae* but from *Streptococcus pyogenes* and *Streptococcus agalactiae*, two distinct and different species of bacteria. In the absence of any experimental evidence comparing any of these sequences for their immunogenicity, mere similarity by *in silico* comparisons are insufficient to support an inference by the skilled worker that sequences from *Streptococcus pyogenes* and *Streptococcus agalactiae* would exhibit immunogenicity against antigens from *Streptococcus pneumoniae*.

In addition, the Action asserts that SEQ ID NO 4652 disclosed in WO 02/077021 is a homologue of the GBS65 protein from *Streptococcus agalactiae* (identified as SEQ ID NO 8544 from PCT/GB01/04789, shown in Table IV thereof). A sequence comparison, appended hereto as Exhibit A, between SEQ ID NO 4652 disclosed in WO 02/077021 and SEQ ID NO 8544 from

McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive
Chicago, IL 60606
Telephone: (312) 913-0001
Facsimile: (312) 913-0002

PCT/GB01/04789 reveals only 44% amino acid sequence identity, a value that the skilled worker would consider inconsistent with the interpretation asserted by the Office.

The immunogenic capacity of SEQ ID NO 8544 from PCT/GB01/04789 is also inconsistent with the Office's interpretation of this reference. As shown in Example 313 of the secondary reference (pp. 397-399 of the published international application, No. WO 02/34771) and in Table III (p. 2991), the difference in immunoreactivity between pre- and post-immune sera using SEQ ID NO. 8544 as an immunogen corresponds to about 20% protection from immune challenge. Applicants respectfully submit that the skilled worker would interpret these results to mean that SEQ ID NO. 8544 would provide just a very limited level of protection, and would be unsuitable as a vaccine due to its weak protective activity.

Applicants thus respectfully contend that the uncertain homology between proteins from distinct bacterial species and the weak immunogenicity of said putative homologous peptides would not have permitted the skilled worker to form a reasonable expectation of successfully achieving the claimed invention. Moreover, the skilled worker would recognize that the cited art does not disclose the specific antigenic peptides and polypeptides disclosed in their specification, and thus does not anticipate their pending claims. They respectfully request that the Examiner withdraw these grounds of rejection.

CONCLUSION

Applicants respectfully contend that the instant application is in condition for allowance in view of the claim amendments and arguments presented above, and respectfully requests it be allowed. If the Examiner believes that a telephone or personal interview would expedite prosecution of the instant application, the Examiner is respectfully invited to call the undersigned attorney at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff LLP

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By: /Kevin E. Noonan/
Kevin E. Noonan, Ph.D.
Reg. No: 35,303

McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive
Chicago, IL 60606
Telephone: (312) 913-0001
Facsimile: (312) 913-0002